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Original article

Right internal thoracic artery or radial artery: A propensity matched comparison on the second best arterial conduit

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Abbreviations

AF: atrial fibrillation BMI: body mass index

CABG: coronary artery bypass grafting

COPD: chronic obstructive pulmonary disease

DM: diabetes mellitus

CVA: cerebrovascular accident

CX: circumflex artery

DIA: diagonal

IABP: intra-aortic balloon pump

LAD: left anterior descending artery

LITA: left internal thoracic artery

LMS: left main stem

LVEF: left ventricular ejection fraction

MI: myocardial infarction

OPCAB: off-pump coronary artery bypass grafting

PCI: percutaneous coronary intervention

PSM: propensity score matching

PVD: peripheral vascular disease

RA: radial artery

RCA: right coronary artery

RCT: randomized controlled trial

RITA: right internal thoracic artery

RRT: renal replacement therapy

SMD: standardized mean difference

SW: sternal wound

Abstract (*Word count: 239)*

Objective(s): We conducted a propensity score matching to determine whether the use of the right internal thoracic artery (RITA) confers a survival advantage when compared to the radial artery (RA) as second arterial conduit in coronary artery bypass grafting (CABG).

Methods: The study population included a highly selected low risk group of patients who received the RITA (n=764) or the RA (n=1990) as second arterial conduit. We obtained 764 matched pairs that were comparable for all pre-treatment variables. Time-segmented Cox regression model that stratified on the matched pairs was used to investigate the effect of treatment on late mortality.

Results: After a mean follow-up of 10.2±4.5 years (max 17.3 years), survival probabilities at 5, 10 and 15 years were 96.4±0.7% versus 95.4±0.7%, 91.0±1.1% versus 89.1±1.2% and 82.4± 1.9% versus 77.2± 2.5% in the RITA and RA groups respectively. During the first 4 years, RITA and RA were comparable in terms of mortality (HR 1.00; 95%CI 0.56-1.78; P=0.98). However, after 4 years RITA was associated with a significant reduction in late mortality (HR 0.67; 95%CI0.48-0.95; P=0.02). RITA was superior to RA when the experimental conduit was used to graft the left coronary system (HR 0.69;95%CI 0.47-0.99; P=0.04) but not the right coronary system (HR 0.98;95%CI 0.59-1.62; P=0.93)

Conclusions: In a highly selected low-risk group of patients, the use of the RITA as second arterial conduit for the left coronary system was associated with better survival when compared to the RA.

Keyword: coronary artery bypass grafting, multiple arterial grafting; propensity score matching ; survival

Central message: In a highly selected low-risk group of patients, the right internal thoracic artery used as second arterial graft for the left coronary system was associated with better survival when compared to the RA.

Perspective Statement: The choice of the right internal thoracic artery or radial artery as second conduit in patients undergoing CABG, remains controversial. In a highly selected low-risk group of patients, the right internal thoracic artery used as second arterial graft for the left coronary system was associated with better survival when compared to the RA.

Despite increasing recognition that multiple arterial conduits improve long-term outcomes following coronary artery bypass grafting (CABG) [1], the quest for the second best arterial conduit to supplement the left internal thoracic artery continues [2]. In particular, whether the use of the right internal thoracic artery (RITA) confers a survival advantage when compared to the radial artery (RA) still needs to be determined [3]. To date, only a single randomized controlled trial (RCT) [3] has been published in the literature, largely underpowered to detect any difference in long term survival between RITA and RA groups. Several observational studies comparing RITA versus RA have been reported with conflicting findings [5-12]. Propensity score matching (PSM) based analysis of observational data is emerging as an attractive alternative in view of paucity of evidence from RCT, and can be relied upon as evidence when RCTs are not possible [4]. Recently general recommendations have been proposed in conducting PSM [13-15]. We aimed to compare short term outcomes and long term survival in patients receiving RITA versus RA as second arterial conduit by conducting a single centre 15 years outcomes PSM comparison in accordance with current recommendations.

Methods

The study was conducted in accordance with the principles of the Declaration of Helsinki. The local audit committee approved the study, and the requirement for individual patient consent was waived. We retrospectively analysed prospectively collected data from The National Institute for Cardiovascular Outcomes Research (NICOR) NACSA registry on 1 June 2015 for all isolated first time CABG procedures performed at the Bristol Heart Institute, Bristol United Kingdom from April 1996 to April 2015. Reproducible cleaning algorithms were applied to the database, which are

regularly updated as required. Briefly, duplicate records and non-adult cardiac surgery entries were removed; transcriptional discrepancies harmonized; and clinical conflicts and extreme values corrected or removed. The data are returned regularly to the local units for validation.

Further details and definition of variables are available at http://www.ucl.ac.uk/nicor/audits/adultcardiac/datasets. Among 15119 isolated first time CABG cases performed during the study period**,** we selected subjects who met the following criteria: multivessel coronary disease including left main and/or left anterior descending (LAD) coronary disease; requiring at least 2 grafts; CABG performed by using the following strategies: left internal thoracic artery (LITA) used as in-situ to graft the LAD territory and RA graft the non-LAD territory with or without additional SV grafts (RA group) or both LITA and RITA with or without additional SV grafts as required in both groups (Supplementary Figure 1). Patients receiving both the RITA and the RA (n=275) were excluded from the present analysis. In the present series, the RITA and the RA were used only in case of target stenosis ≥75%.The RA was used as a free graft directly connected to the ascending aorta. The internal thoracic artery was harvested as a pedicle in all cases and was used as in situ graft that remained proximally connected to its respective subclavian artery or as a free graft proximally connected to other internal thoracic artery.

Pre-treatment variables and study end-points

The effect of adding the RA as third arterial conduit instead of SV was adjusted for the following variables including: age, gender, body mass index (BMI); previous myocardial infarction (MI), previous percutaneous coronary intervention (PCI); diabetes mellitus (DM) orally treated or on insulin; chronic obstructive pulmonary disease (COPD); current smoking; serum creatinine ≥200 mmol/l, previous

cerebrovascular accident (CVA); peripheral vascular disease (PVD); preoperative atrial fibrillation (AF); left main disease (LMD); non-LAD vessel diseased including Diagonal (DIA); circumflex artery (CX); right coronary artery (RCA); left ventricle ejection fraction (LVEF), non elective priority, off-pump coronary artery bypass (OPCAB), procedure performed by resident versus attending surgeon and logistic Euroscore.

Short term outcomes investigated were 30-day mortality, need for post-operative intra-aortic balloon pump (IABP), re-exploration for bleeding, renal replacement therapy (RRT) and sternal wound reconstruction. Long term outcome was all-cause mortality. All-cause mortality is the most robust and unbiased index because no adjudication is required; thus, inaccurate or biased documentation or clinical assessments are avoided [16]. Information about death was obtained from the institutional database and the National General Register Office for all patients. Follow-up was completed for all patients (100%).

Statistical analysis

For baseline characteristics, variables are summarized as mean for continuous variables and proportion for categorical variables. Multiple imputation was used to address missing data (Supplementary Table 1 and Supplementary Figure 2) (http://www.jstatsoft.org/v45/i07/). To control for measured potential confounders in the data set, a propensity score (PS) was generated for each patient from a multivariable logistic regression model based on pre-treatment covariates as independent variables with treatment type (RITA vs RA) as a binary dependent variable according to current recommendations [13,15]. The resulting propensity score represented the probability of a patient receiving the RITA as second arterial conduit.

As the PS model achieved a good discriminatory power C-statistic =0.74; Supplementary Figure 3), no attempt was made to include interactions or non-linear terms. Pairs of patients receiving RITA and RA were derived using greedy 1:1 matching with a calliper of width of 0.2 standard deviation of the logit of the PS [14] (http://CRAN.Rproject.org/package=nonrandom) . The quality of the match was assessed by comparing selected pre-treatment variables in propensity score–matched patient using the standardized mean difference (SMD), by which an absolute standardized difference of greater than 10% is suggested to represent meaningful covariate imbalance [13-15]. Analytic methods for the estimation of the treatment effect in the matched sample were selected. McNemar's was used to compare postoperative complications rate in the two groups [13]. In the primary Kaplan–Meier analysis, comparing late survival between the two groups, it was found that the curves crossed thus showing that the proportional hazards assumption was violated and the hazard was not constant with time. To evaluate the trends in this Kaplan–Meier curve, time-segmented Cox regression models before and after the curves crossed [17] stratified on the matched pairs [18] were used to investigate the effect of treatment (RITA vs RA) on early and late mortality phases. This approach accounts for the within-pair homogeneity by allowing the baseline hazard function to vary across matched sets (http://CRAN.R-project.org/package=survival). Schoenfeld residuals test was used to confirm the non-violation of the proportional hazard assumption in the two separate Cox models. Subgroup analysis on late mortality according to the experimental conduit target, RITA configuration and OPCAB usage was carried out by mains of covariate adjustment using the propensity score on the overall sample to account for the relatively small sample size. Finally, due to the different distribution in OPCAB rate across the years (Supplementary Figure 4), the treatment effect was

adjusted for the interaction between OPCAB and year of surgery. Due to the highly selected low risk population, frailty models were not used. All p-values <0.05 were considered to indicate statistical significance. All statistical analysis was performed using R Statistical Software (version 3.2.3; R Foundation for Statistical Computing, Vienna, Austria).

Results

The study population included 764 low-risk subjects who received RITA with (n=482) or without (282) additional SV grafts and 1990 subjects who received the RA with (n=1206) or without (784) additional SV grafts. Patients characteristics distribution before and after PS matching are summarized in Table 1. In the unmatched group, RA tended to present a higher burden of comorbidities. In particular they were more likely to be older and female and to have a BMI ≥30, COPD and diabetes (both orally treated and on insulin) and impaired left ventricular function. OPCAB rate was higher in the RA group (video 1). After matching the 764 matched pairs groups were comparable for all pre-treatment variables (SMD<10, Figure 1).

Arterial graft configuration

Mean number of graft performed were 2.87±0.76 in the RITA group versus 2.80±0.70 and 2.87±0.70 in the unmatched (P=0.003) and matched (P=0.1) RA groups respectively. Grafts target in the unmatched and matched groups are summarized in Table 2. The RITA was used to graft the CX territory in 319(42%), the RCA territory in 245(32%) cases and the LAD territory in 200 (26%) cases. Overall, the CX territory was grafted by using an internal thoracic artery in 519(68%) cases The RA was used to graft the CX territory in 1530(77%) and 565(74%), the RCA territory in 460(23%) and 199 (26%) cases in the unmatched and matched RA groups respectively. RITA was used as a Y-graft in 144 cases and as in-situ graft in the remaining 620 cases.

Short term outcomes

Short term outcomes in the matched samples are summarized in Table 2. The two groups were comparable in terms of 30-day mortality, incidence of cerebrovascular accident, need for renal replacement therapy. However, we found a trend towards a higher rate of re-exploration for bleeding, sternal wound reconstruction and need for postoperative IABP in the RITA group, although the overall incidence of these complication was relatively low. Hospital stay length tended to be increased in the RITA group. Short term outcomes in the unmatched RA group is reported in Supplementary Table 2.

Mortality

In the PS matched group, mean time to follow-up was 10.2±4.5 years (max 17.3 years) and 10.1±5.1 years and 10.3±3.7 in the RITA and the matched RA group respectively (P=0.31). A total of 85 and 106 deaths in the RITA and RA groups respectively were recorded. Survival probabilities at 5, 10 and 15 years were 96.4±0.7% versus 95.4±0.7%, 91.0±1.1% versus 89.1±1.2% and 82.4± 1.9% versus 77.2± 2.5% in the RITA and RA groups respectively. The two survival curves crossed at 4 years (96.9±0.6 respectively, Figure 2). During the first 4 years, RITA and RA were comparable in terms of mortality (HR 1.00; 95%CI 0.56-1.78; P=0.98). However, after 4 years RITA was associated with a significant reduction in late mortality (HR 0.67; 95%CI0.48-0.95; P=0.02). Schoenfeld residuals test excluded proportional hazard assumption violation (P=0.93, Supplementary Figure 5).Survival rate in unmatched RA group is reported in Supplementary Figure 6.

Subgroup analysis on late mortality (after 4 years)

Subgroup analysis suggested that RITA was superior to RA in term of late survival when the experimental conduit was used to graft the left coronary system (HR

0.69;95%CI 0.47-0.99; P=0.04) but not the right coronary system (HR 0.98;95%CI 0.59-1.62; P=0.93) (Figure 3). In cases with the experimental conduit grafted on the right coronary system only, neither in-situ RITA (HR 0.76; 95%CI 0.42-1.36; P=0.1) or free RITA (HR 1.78; 95%CI 0.89-3.56; P=0.3) were significantly associated with a better late survival when compared to the RA (Supplementary Figure 7).

On the other hand, in cases with the experimental conduit grafted on the left coronary system only, we could not demonstrate any significant difference between free-RITA over in-situ RITA (HR 0.55; 95%CI 0.21-1.43; P=0.22; Figure 4). No significant difference in late mortality could be demonstrated between RITA grafted to the circumflex artery (with LITA to LAD) when compared to RITA grafted to the LAD territory (with LITA to circumflex artery) (HR 0.71;95%CI 0.34-1.43; P=0.33). When subjects receiving sequential grafts were excluded, the use of RITA to graft the left coronary system was still found to be superior to the RA (HR 0.65; 0.43-0.99; P=0.04). Finally the protective effect of RITA over RA on late mortality was confirmed when adjusted for the interaction between OPCAB and era of surgery (HR 0.73; 95%CI 0.54-0.99; P=0.04).

Discussion

The present single centre long term PSM analysis, showed that in a low risk population, the use of the RITA when compared with the RA as second arterial conduit was associated with superior long term survival in patients undergoing CABG. This trend became to appear evident beyond 4 years. However, we found that the superiority of the RITA was evident only when the experimental conduit was used to graft the left coronary system. When used to graft the left coronary system free RITA and in-situ RITA showed comparable long term survival. Survival after RITA to LAD graft did not significantly differ from RITA to circumflex artery graft.

The use of RITA over the RA did not significantly increase operative mortality (within 30 days) and the incidence of postoperative cerebrovascular accident or need for renal replacement therapy. However, we found a trend towards an increased incidence of re-exploration for bleeding, IABP requirement and sternal wound complication requiring reconstruction in patients receiving the RITA. However, the overall incidence of these complications was relatively low partially due to the low risk profile of the study population.

In spite of a slow initial adoption, multiple arterial grafting is now widely advocated by the cardiovascular community [1]. The use of both RITA and RA has been showed to be associated with better long term survival when compared to the traditional strategy with a single internal thoracic artery and additional saphenous vein grafts [9]. Controversy still remains, on whether the use of the RA as second arterial conduit achieves the same long-term benefits as that documented with the use of the RITA [5-12]. The lack of clear evidence, the potentially increased sternal wound complication rate and the perceived technical complexity by using bilateral internal thoracic arteries often result in the RA as the preferred second conduit of choice [1]. The only randomized direct comparison in the literature is the Radial Artery Patency and Clinical Outcome (RAPCO) [3] which randomized 196 patients to the RITA and 193 patients to the RA. At midterm follow-up no significant differences in terms of angiographic patency and clinical outcome were found. However, the trial was largely underpowered to detect significant differences in survival between the two groups.

PSM is emerging as an attractive alternative in view of paucity of evidence from RCT [4]. Recently, conflicting results have been reported on the superiority of the RITA over the RA from several PSM studies. Schwann et al. [9] reported on 551 propensity matched RITA and RA their conclusions supported the equipoise between RITA and

RA as the best-second arterial conduit. However, it should be noted that their analysis showed a clear trend towards a better survival by using RITA over RA (HR 1.35 0.98–1.81). Shi et al. [10] performed a PSM on 318 matched pairs of patients receiving RITA versus RA. They demonstrated a marginally significant survival benefit from RITA (HR 0.78; 95%CI 0.60-1.00; P=0.048). On the contrary, Tranbaugh et al [11], reported on 528 pairs who received either a RA a free RITA to bypass the circumflex coronary. Ten-year survival was 85% for RA and 80% for RITA patients, which was not statistically significant (P=0.06) RA patency (83.9%) was similar to RITA patency (87.4%) (P= 0.15).It should be noted that in their series, the RITA was used as free graft directly connected to the aorta in 42% of cases and the mismatch in calliper between the aorta and the RITA might have affected its patency thus abolishing any survival advantage.

By conducting a single centre 15 years PSM on 764 pairs of patients receiving RITA versus RA as second arterial conduit, we found that the use of the RITA is associated with a significant risk reduction of mortality after 4 years but this benefit is more likely to be relevant only when the RITA is used to graft the left coronary system. These findings are supported by previous studies which suggested that for bilateral ITA grafting to improve long-term outcomes over single ITA-to-LAD grafting, the second ITA should bypass the circumflex artery rather than the right coronary artery [19-21]. Schmidt and colleagues [19] observed long-term survival of 93% when both ITAs were used to bypass left-sided coronary arteries but only 70% when grafted to the RCA system after a mean follow-up of 9.2 years (*P*=0.02). Carrel [20] and Pick [21] have separately reported that using both ITAs to graft left-sided coronaries may increase survival over single ITA revascularization. These observations may reflect the lower patency of ITA grafts when used to bypass the RCA system compared with left-sided

coronary arteries. Grafts to the three different coronary artery territories have different patency rates which have been clearly demonstrated for individual ITA grafts [22]. Robinson et al [23] recently reported on postdischarge angiography of 296 free RITA as y graft including a total of 1,174 individual anastomoses examined. There were 428 anterior wall (36.5%), 411 lateral wall (35.0%), and 335 inferior wall (28.5%) anastomoses. The patency rates for these were 90.6%, 83.9%, and 62.3%, respectively.

In contrast, Kurlansky et al. [24] compared 1,479 RITA used to revascularize the left coronary system versus 736 RITA used to graft the right coronary system and they found similar survival after a mean follow-up of 12 years. In their series, in-situ grafting was used in the majority of cases (approximately 98% of arteries grafted) and when using the RITA to the right coronary artery, efforts were made to graft severely stenosed vessels and distal branches rather than the main RCA. In this context, Sabik at al. [25] were able to document equivalent long-term results with the use of the RITA, whether applied to the left or right coronary system. Their findings of similar survival whether the RITA was used to bypass the RCA or Cx system were attributable to careful patient selection. In fact, two important factors used in selecting the right coronary artery as the site for the RITA were (1) stenosis 70% to 90% with viable myocardium in its distribution; and (2) freedom from distal stenosis. Therefore they were likely to graft a RCA with RITA only when the likelihood of the RITA graft remaining patent, and therefore effective, was high.

We could not demonstrate a superiority of in-situ over y graft RITA configuration when RITA was used to graft the left coronary system. This result is supported a recent 5-year angiographic follow-up by Hwang et al. [26] on 398 patients who underwent OPCAB with in-situ RITA (n=164) graft or free RITA Y-composite graft (n=234) used

to graft the left coronary system. They found that 5-year patency rate was 92.5% vs 92.4% for in-situ RITA and free RITA graft respectively (p=0.97). Finally, we found that in situ RITA to LAD was a valid alternative to in situ LITA to LAD when performing CABG using bilateral ITAs grafting on the left coronary system being associated with similar survival rates. RITA to LAD strategy represents an easily reproducible and technically less demanding strategy compared with other configurations. The RITA is biologically identical to the LITA and excellent angiographic results have been reported for RITA to LAD grafts [22]. Tatoulis and colleagues [27] reported a 95% 10-year patency rate for 149 RITA to LAD grafts and this result was comparable with LITA to LAD grafts (96%). In a previous series, we have demonstrated similar survival rate and freedom from re-intervention between RITA to LAD versus LITA to LAD in the context of bilateral ITA grafting [27].

Although in this low risk population, operative complication were particularly low in both groups, the use of RITA was associated6 with an increased surgical morbidity including increased risk of re-exploration for bleeding, need for intra-aortic balloon pump and sternal wound reconstruction and prolonged hospital stay length. Inability to control bleeding from branches of the retrocaval and retroaortic routed RITA, which are in spasm at the time of closure and bleed later because of vasodilatation, as well as an increased number of potential bleeding sites due to construction of the Y-graft are some of the plausible reasons for the higher rate of re-exploration in the RITA group [28]. Moreover, retrocaval and transverse sinus routing of the RITA might compromise graft flow because of undetected kinks, graft overstretching, and rotation, which can partially account for the increased need of IABP [28]. Finally the use of RITA was confirmed to increase the risk of sternal wound reconstruction. In the present series a pedicled harvesting technique was used in all cases and this might account for this result and better results are anticipated by using skeletonized technique [29]. Taking into account the observed increased operative morbidity associated with the

RITA and based on the observation that the beneficial impact on survival from the RITA may be delayed by as much as 7 to 10 years [30], it seems reasonable to consider the RA as a valid option in older patients or patients with greater number of risk factors such as diabetes, obesity [31].

The present analysis has intrinsic limitations. The main limitation of our study is that no follow-up data were available to compare the groups with respect to the cause of death (cardiac vs noncardiac), recurrence of angina, need for repeated revascularization, and graft patency. Therefore we can only speculate that the mechanism beyond the better long-term survival observed in our RITA group is related to the better patency rate of the RITA over the RA. Propensity technique can adjust only for measurable and included variables and we cannot exclude a selection bias based on non-measurable "eye-ball" variables (with the RITA reserved to healthier and better patients).

In conclusion, we found that in a highly selected low-risk group of patients, the use of the RITA as second arterial conduit for the left coronary system was associated with better survival when compared to the RA.

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Table 1. Pre-treatment variables distribution in the RITA group and in the unmatched and matched RA group

		RIMA N=764		unmatched RA N=1990		PSM RA N=764		SMD before PSM	SMD after PSM
		n	%	n	%	n	%		
Age	mean,ds	57±9		61±9		58±8		-44.6	-4.1
	<60	501	65.6	859	43.2	453	59.3		
	60-69	213	27.9	797	40.1	254	33.2		
	70-79	41	5.4	303	15.2	55	7.2		
	≥80	9	1.2	31	1.6	2	0.3		
Female	No	710	92.9	1727	86.8	711	93.1	-20.5	-0.5
	Yes	54	7.1	263	13.2	53	6.9		
BMI	mean,sd	28±3		29±4		28±4		-23.7	-2.9
	<30	597	78.1	1318	66.2	568	74.3		
	≥30	167	21.9	672	33.8	196	25.7		
MI	No	447	58.5	1096	55.1	443	58.0	-6.9	-1.1
	Yes	317	41.5	894	44.9	321	42.0		
PCI	No	725	94.9	1883	94.6	726	95.0	1.2	0.6
	Yes	39	5.1	107	5.4	38	5.0		
DM	no	725	94.9	1635	82.2	715	93.6	-35.4	-1.1
	Orally treated	17	2.2	212	10.7	34	4.5		
	On insulin	22	2.9	143	7.2	15	2.0		
Current Smoking	No	631	82.6	1677	84.3	621	81.3	-4.5	-3.4
	Yes	133	17.4	313	15.7	143	18.7		
Creatinine>200mmol/l	No	760	99.5	1986	99.8	763	99.9	5.4	6.9
	Yes	4	0.5	4	0.2	1	0.1		
COPD	No	726	95.0	1813	91.1	728	95.3	-15.5	-1.2
	Yes	38	5.0	177	8.9	36	4.7		
CVA	No	754	98.7	1939	97.4	752	98.4	-9.1	-2.2
	Yes	10	1.3	51	2.6	12	1.6		
PVD	No	716	93.7	1853	93.1	718	94.0	2.4	1.1
	Yes	48	6.3	137	6.9	46	6.0		

AF	No	754	98.7	1938	97.4	752	98.4	-9.4	-2.2
	Yes	10	1.3	52	2.6	12	1.6		
LVEF	≥50%	646	84.6	1587	79.7	647	84.7	-13.4	0
	30%-49%	109	14.3	359	18.0	107	14.0		
	<30%	9	1.2	44	2.2	10	1.3		
Preoperative IABP	No	763	99.9	1988	99.9	763	99.9	-0.9	0
	Yes	1	0.1	2	0.1	1	0.1		
OPCAB	No	421	55.1	617	31.0	380	49.7	-50.2	-9.8
	Yes	343	44.9	1373	69.0	384	50.3		
Non elective priority	No	427	55.9	1176	59.1	421	55.1	6.5	1.6
	Yes	337	44.1	814	40.9	343	44.9		
Performed by resident	No	419	54.8	1423	71.5	435	56.9	35.1	4.2
	Yes	345	45.2	567	28.5	329	43.1		
Logistic EuroSCORE	mean,sd	2%±2%		2%±3%		2%±2%		-19.2	-0.7
	<1.0%	233	30.5	369	18.5	220	28.8		
	1.0%-1.9%	318	41.6	816	41.0	336	44.0		
	2%-2.9%	114	14.9	391	19.6	124	16.2		
	≥3.0%	99	13.0	414	20.8	84	11.0		
Year of surgery	1996-1999	289	37.8	160	8.0	99	13.0	-33.3	-7.8
	2000-2004	190	24.9	743	37.3	338	44.2		
	2005-2009	133	17.4	835	42.0	274	35.9		
	2010-2015	152	19.9	252	12.7	53	6.9		
LMD	No	587	76.8	1502	75.5	576	75.4	3.2	3.4
	Yes	177	23.2	488	24.5	188	24.6		
LAD	No	4	0.5	25	1.3	4	0.5	7.8	0
	Yes	760	99.5	1965	98.7	760	99.5		
RCA	No	220	28.8	701	35.2	220	28.8	13.8	0
	Yes	544	71.2	1289	64.8	544	71.2		
CX	No	151	19.8	379	19.0	136	17.8	1.8	5
	Yes	613	80.2	1611	81.0	628	82.2		
DIA	No	599	78.4	1511	75.9	598	78.3	-5.9	-0.3
	Yes	165	21.6	479	24.1	166	21.7		

RITA: right internal thoracic artery; RA: radial artery; PSM: propensity score matched; SMD: standardized mean difference; BMI: body mass index; MI: myocardial infarction; PCI: percutaneous coronary intervention; DM: diabetes mellitus; COPD: chronic obstructive pulmonary disease; CVA: cerebrovascular accident; PVD: peripheral vascular disease; AF: atrial fibrillation; LVEF: left ventricular ejection fraction; IABP: intra-aortic balloon pump; LMS: left main stem; LAD: left anterior descending artery; RCA: right coronary artery; CX: circumflex artery; DIA: diagonal; OPCAB: off-pump coronary artery bypass grafting.

Table 2. Arterial graft target and configuration

RITA target **(N=**764)	**RA target Unmatched** **(N=**1990)	**RA target Matched** **(N=**764)
RCA as in-situ graft=198(26%)* RCA as free graft=47(6%)*† CX as in-situ graft (retro-aortic)=232(31%)* CX as free graft=87(11%)*† LAD as in-situ graft =190(25%)‡ LAD as free graft=10(1%)†‡ sequential grafts=46(6.0%)	RCA=460(23%)* CX=1530(77%)* sequential grafts=130(6.5%)	RCA=197(26%)* CX*=567(74%)* sequential grafts=46(6.0%)

* LITA has been used to graft the LAD as in-situ graft; †RITA proximally connected to the LITA (y graft); ‡LITA has been used to graft the CX as in-situ graft

RITA: right internal thoracic artery; RA: radial artery; LITA: right internal thoracic artery; CX: circumflex artery; RCA: right coronary artery.

Table 3. Short term outcomes

		RIMA N=764		PSM RA N=764		P-value
		n	%	n	%	
Mortality within 30 days	No	758	99.2	762	99.7	0.26
	Yes	6	0.8	2	0.3	
Re-exploration for bleeding	No	737	96.5	753	98.6	0.01
	Yes	27	3.5	11	1.4	
Postoperative CVA	No	759	99.3	759	99.3	1
	Yes	5	0.7	5	0.7	
Postoperative RRT	No	752	98.4	758	99.2	0.24
	Yes	12	1.6	6	0.8	
Postoperative IABP	No	754	98.7	762	99.7	0.04
	Yes	10	1.3	2	0.3	
SW reconstruction	No	757	99.1	763	99.9	0.07
	Yes	7	0.9	1	0.1	
Length of hospital stay	mean±sd	7.1±5.1		6.6±3.7		0.05
	[2,10)	676	88.5	691	90.4	
	[10,75]	88	11.5	73	9.6	

RITA: right internal thoracic artery; RA: radial artery; PSM: propensity score matched; CVA: cerebrovascular accident; RRT renal replacement therapy; IABP: intra-aortic balloon pump; SW: sternal wound

Supplementary Table 1. Missing data rate

Variable	Count	%
Age	0	0%
Female	0	0%
MI	12	0.4%
PCI	5	0.2%
DM	10	0.4%
Current smoking	9	0.3%
Creatinine>200 mmol/l	8	0.3%
COPD	9	0.3%
CVA	24	0.9%
PVD	9	0.3%
AF	8	0.3%
LMD	203	7.3%
LVEF	27	0.9%
Preoperative IABP	17	0.6%
OPCAB	40	1.4%
Non elective priority	1	0.03%
BMI	198	7.1%
Performed by resident	1	0.03%
Logistic EuroSCORE	0	0%
Year Of Surgery	0	0%
LAD	0	0%
DIA	0	0%
CX	0	0%
RCA	0	0%

BMI: body mass index; MI: myocardial infarction; PCI: percutaneous coronary intervention; DM: diabetes mellitus; COPD: chronic obstructive pulmonary disease; CVA: cerebrovascular accident; PVD: peripheral vascular disease; AF: atrial fibrillation; LVEF: left ventricular ejection fraction; IABP: intra-aortic balloon pump; LMS: left main stem; LAD: left anterior descending artery; RCA: right coronary artery; CX: circumflex artery; DIA: diagonal; OPCAB: off-pump coronary artery bypass grafting.

Figure legend

Central picture. Kaplan-Meier survival curve probabilities in the right internal thoracic artery (RITA) and the radial artery (RA) groups in the propensity score matched population.

Figure 1. Graphical visualization of standardized mean difference before after propensity score matching

(BMI: body mass index; MI: myocardial infarction; PCI: percutaneous coronary intervention; DM: diabetes mellitus; COPD: chronic obstructive pulmonary disease; CVA: cerebrovascular accident; PVD: peripheral vascular disease; AF: atrial fibrillation; LVEF: left ventricular ejection fraction; IABP: intra-aortic balloon pump; LMS: left main stem; RCA: right coronary artery; CX: circumflex artery; DIA: diagonal; OPCAB: off-pump coronary artery bypass grafting).

Figure 2. Kaplan-Meier survival curve probabilities in the right internal thoracic artery (RITA) and the radial artery (RA) groups in the propensity score matched population.

Figure 3. PS-adjusted Cox model survival curve probabilities in the right internal thoracic artery (RITA) and the radial artery (RA) groups according to the experimental conduit target

Figure 4. PS-adjusted Cox model survival curve probabilities in the right internal thoracic artery (RITA) and the radial artery (RA) groups with the experimental conduit grafted to the left coronary system according to different RITA graft configuration.

Supplementary Figure 1. Number of procedures per year performed by using the RITA or the RA as second arterial conduit during the study period. (RITA: right internal thoracic artery; RA: radial artery)

Supplementary Figure 2. Graphical visualization of missing data rates and combinations

Supplementary Figure 3. Area under the curve for the Propensity Score model

Supplementary Figure 4. Number of procedures per year performed off-pump during the study period (OPCAB: off-pump coronary artery bypass; ONCAB: on-pump coronary artery bypass)

Supplementary Figure 5. Schoenfeld residuals visualization to check the proportional hazard assumption for the treatment variable on late mortality (beyond 4 years).

Supplementary Figure 6. Kaplan-Meier survival curve probabilities in the unmatched radial artery (RA) groups.

Supplementary Figure 7. PS-adjusted Cox model survival curve probabilities in the right internal thoracic artery (RITA) and the radial artery (RA) groups with the experimental conduit grafted to the right coronary system according to different RITA graft configuration.

Video 1. Radial artery grated to the circumflex artery during off-pump coronary artery bypass